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DOCKET NO. ORT-1230

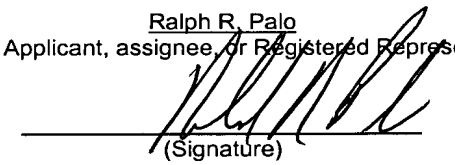
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	S. Dax *et al.*		
Serial No.:	09/552,969	Art Unit :	1624
Filed :	April 20, 2000	Examiner:	Hong Liu
Title :	3a,4,5,9b-tetrahydro-1h-benz[e]indol-2yl amine-derived neuropeptide y receptor ligands useful in the treatment of obesity and other disorders		

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington D.C. 20231 on

February 11, 2004
(Date of Deposit)

Ralph R. Palo
Name of Applicant, assignee, or Registered Representative



(Signature)

February 11, 2004
(Date of Signature)

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.131

Dear Sir:

1. We, Scott L. Dax and James McNally declare that we are the inventors of the invention described and claimed in U.S. patent application Serial No. 09/522,969, filed on April 20, 2000, which application is based on provisional application Serial No. 60/132,660, filed May 5, 1999, and now abandoned.

2. We are presently, and were at and before completion of the invention, in the employ of Johnson & Johnson, which is the parent company of Ortho-McNeil Pharmaceutical Corporation, the assignee of record of the entire right, title and interest in the above-identified application.

3. We are familiar with the Office Action dated June 6, 2003 in which the above referenced application was rejected over a publication by McNally et al. which appeared in Bioorganic and Medicinal Chemistry Letters 10 (2000) 213-216.

4. We declare that the invention described and claimed in the above identified application was conceived by us in this country prior to February 7, 2000 and that such conception was coupled with due diligence by us in this country from just prior to February 7, 2000 to a reduction to practice of the invention.

5. Exhibits A-E attached hereto consist of true copies from which the dates have been removed of documents from the Ortho-McNeil Pharmaceutical Corporation research laboratories which record the generic conception of the invention.

6. Exhibits F-AA attached hereto consist of true copies from which the dates have been removed of documents from the Crystalytics Company which illustrate the reduction to practice of the invention.

7. Exhibits AB-AQ attached hereto consist of true copies from which the dates have been removed of documents from the Ortho-McNeil Pharmaceutical Corporation research laboratories which illustrate the operativeness of the invention. The assays and methods employed are known procedures which were published prior to February 7, 2000.

8. All of the above procedures and tests were carried out by us or at our direction from a period prior to February 7, 2000 to a reduction to practice of the invention. The results of the testing indicated that the compounds were useful in the treatment of obesity and other disorders.

9. We, Scott L. Dax and James McNally, further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 2/10/2004

SCOTT L. DAX

Date: 2/10/2004

JAMES MCNALLY

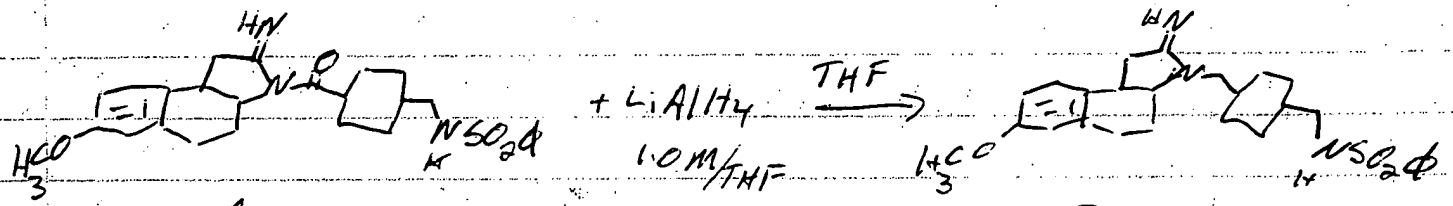
Exhibit A

No. 14794- 65

Project No. 1227 Protocol / Experiment No. ..... Date ..

Subject ..... Purpose .....

Contd. from page _____ .....



1 2 3

	1	2	3
MW	495.64	—	441.66 / 518.13
Wt	1.6g		1.38
mmol	3.22	16.1	
Vol		16.1	

from iPA/iPA/HCl

trit in Et_2O ~75% 3.40

HPLC 3.306 + impurities 8.44

MS 482 MH+

Procedure

In a 200 mL RBF (mag stir, cond., Ar, heat mantle) 1 1.6g was added in portions to a solution of LAH (1.0M in THF 16.1mL) in THF 20mL at rt. Considerable foaming. Rxn heated to reflux 45 min., cooled in ice bath quenched with water 0.65 mL in THF ~5mL, 10% NaOH 0.65 mL then water 2.0mL. stir rt ½h. Added Na_2SO_4 stir 1h. Filter through celite - wash with THF then DCM. Combined organics stripped, residue taken up in iPA ~ 20mL treated with HCl/iPA. No crystallization. Solvent ~~Sample~~ was evap under a stream of N_2. Residue triturated in Et_2O to give a pale pink solid 14794-65-1 1.38g NMR, IR, MS, HPLC

Contd. on page 67 Investigator _____ Date _____

Read and Understood _____ Date _____

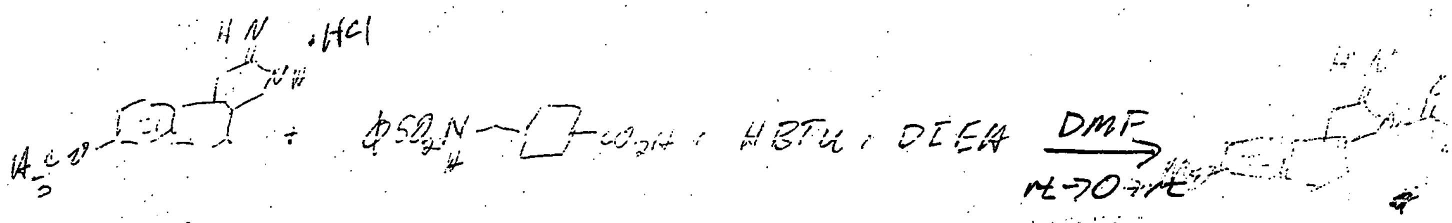
No. 14794- 62

Exhibit B

Project No. 1227 .... Protocol / Experiment No. .... Date

Subject .... Purpose ....

Contd. from page ______



	1	2	3	4	5
MWt	252.75	279.38	379.25	129.25	495.64
Wt	1.0	1.16	1.58	1.79	1.87 g
mmol	3.96	4.15	4.15	13.8	~~4.02~~ 3.7
Vol				2.41	
den				0.742	

496 M+

HPLC 3.214

Procedure

In a 100 mL RBF (mag stir, Ar) DIEA 2.4[illegible] was syringed into a solution of 2 1.16 g & 3 1.58 g in DMF 15 mL at rt. Rxn stirred rt 15 min then cooled to 0°C added 1 1.0 g [illegible] [illegible] products [illegible] Rxn stirred [illegible] [illegible] concentrated [illegible] [illegible] [illegible] [illegible] [illegible] [illegible] triturated in ether. [illegible] with H2O [illegible] in vacuo to give 14794-62-1 1.67 g MS✓ HPLC✓ NMR✓

Contd. on page ______ Investigator [signature] Date ______

[illegible] Understood [signature] Date ______

Exhibit C

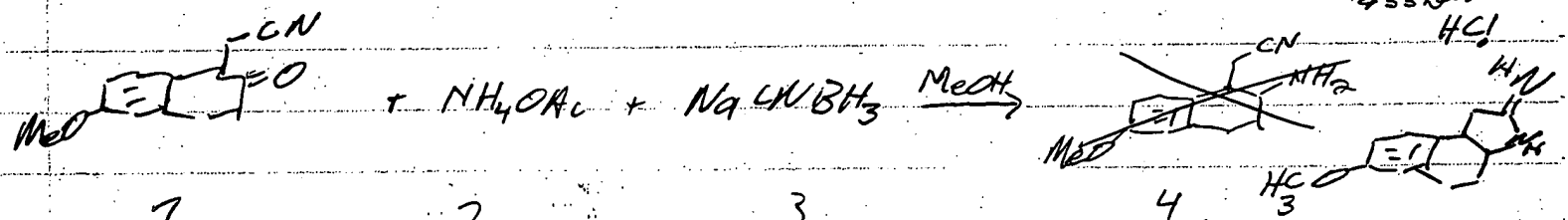
No. 14794- 61

Project No. 6223 Protocol / Experiment No. Date

Subject Purpose RWJ 355295-002-A JMC

Contd. from page

tent. struct. assignment



1 2 3 4

	1	2	3	4
mwt	215.25	77.08	62.84	216.29 / 252.75
wt	~~3.48~~ 3.5 g	~~17.2~~ 18.8	5.11	
mmol	~~16.2~~ 16.2	0.24 mol	81.3	
Vol			50mL	HPLC 1.99 ~ 99%

Procedure

In a 200 mL RBF (mag stir, Ar) a solution of 1 3.5 g & 2 18.8 g in MeOH 50mL was stirred at 15 min. Added 3 5.11 g & heated reflux 5 hr 1h. HPLC - rxn complete Rxn conc. in vacuo at rt. - Treated with NaOH/H2O 12g in 100mL at 0°C. Pale grey solid collected by filtration, wash H2O Air dried - trit. in Et2O filter - air dry to give the free base 14794-61-FB ~~4.5~~ 3.5g - removed 1/2 g store freezer

Remainder dissolved in THF/MeOH ~ 9/1 ~ 75 mL. (need gentle heat to dissolve) add 1N HCl/Et2O ~40mL cool on ice bath filter wash Et2O air dry 14794-61-1 HCl salt 1.571 g

Contd. on page Investigator Date

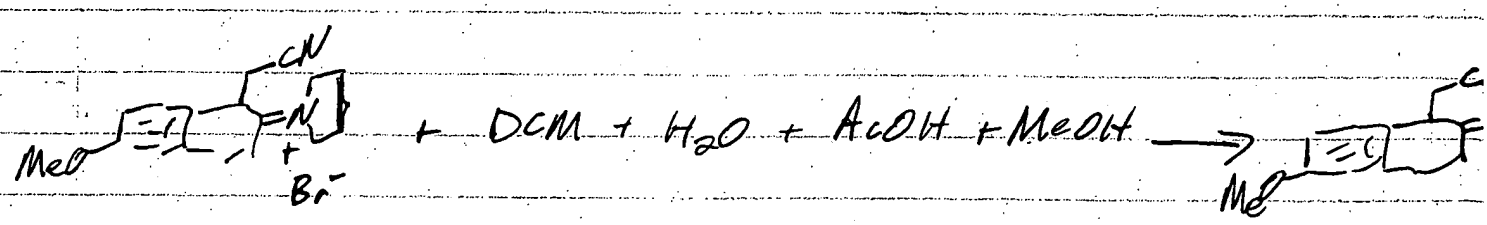
Read and Understood Date

Exhibit D

Project No. 1227 Protocol / Experiment No. Date

Subject Purpose

Contd. from page 59



	1	2	3	4	5	6
MWt						215.25
Wt						3.3g
mmol						
Vol		60	50	5	100	HPLC 2.864

Procedure

In a 500 mL RBF (mag, stir, Ar) 1 (see p. 69) was taken up in DCM 60mL, H_2O 50mL, AcOH 5mL & MeOH 100mL. Resultant soln stirred rt 18h. Rxn complete by LC. Partitioned between DCM 100mL, H_2O 200mL. ~~wash~~ extr. Aq with DCM ~ 100mL. Combined organics wash w H_2O 2x100mL, sat'd $NaHCO_3$ 100mL - dried over $MgSO_4$ & stripped to give a brown oil 14794-60-3.3g HPLC ✓

Contd. on page Investigator Date

Read and Understood Date

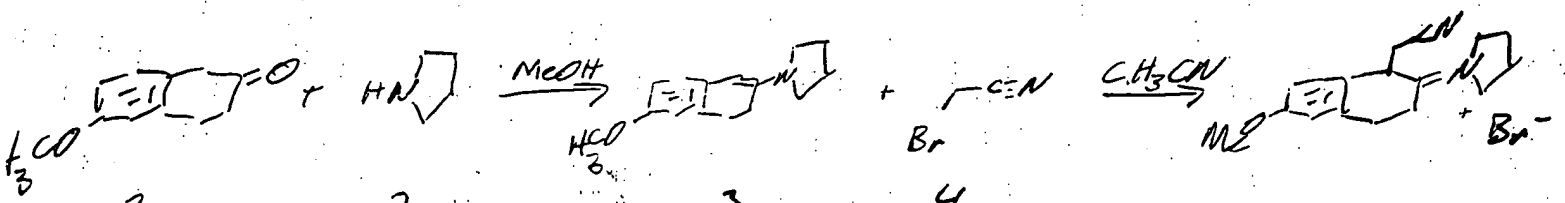
Exhibit E

No. 14794- 59

Project No. 1227 Protocol / Experiment No. ..... Date .....

Subject ..... Purpose See 14139-173 Som NMR 3

Contd. from page _____



	1	2		3	4	
MW	176.22	71.12	→	229.32	119.95	
g	5.64	2.95		5.6 g 76%	3.8	
mol	32.0	41.6		24.4	31.7	
ml		3.5	60		2.21	60
eq		0.850		HPLC 0.933	1.722	

Procedure

In a 300mL RBF (Ar, mag stir) 2 3.5mL was added to a solution of 1 5.64g in MeOH 60 mL. Rxn stirred rt 1-5h. Solid ppt'd. Rxn mix cool in iPA/ice bath. Solid collected by filtration, wash cold MeOH and dried. 14794-59-1 HPLC ~

Solid taken up in CH_3CN ~60mL (mag stir, RT) treated with 4 2.21mL stir rt 1h. Sol'd ppt collected by filtration - wash with CH_3CN, Et_2O - 14794-59-2 HPLC 0.990 @ 2.812 M+ 269

Second crop (HPLC ~) collected & used with 14794-59-2 on p. 60

Contd. on page 60 Investigator _____ Date _____

Read and Understood _____ Date _____

Jim McNally

Exhibit F

CRYSTAL STRUCTURE ANALYSIS REPORT and TABLES for

$[C_{27}H_{36}N_3O_3S][Cl]$

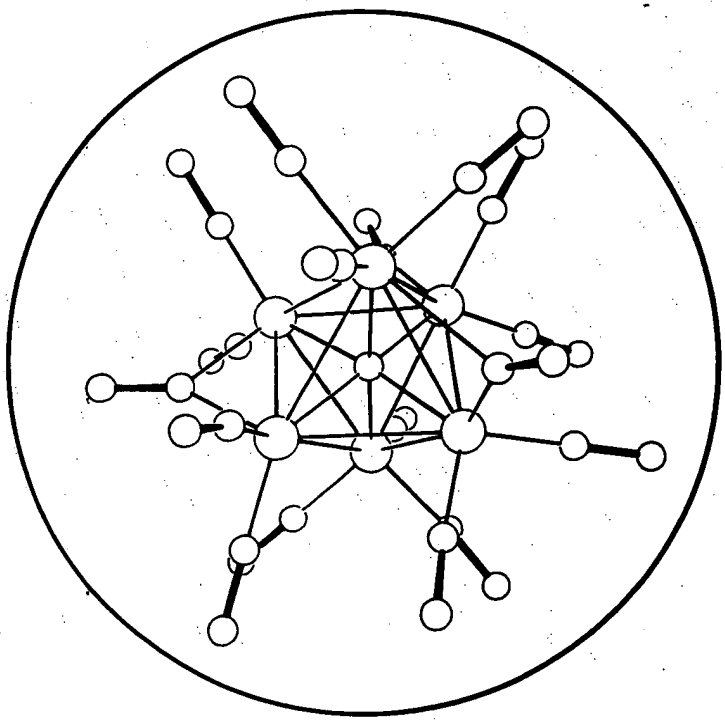
Crystalytics Company Reference Code: **CFS4-0799**

For: The R. W. Johnson Research Institute

Sample #14794-65-1

Jim McNally

Copy 2



CRYSTALYTICS COMPANY

CRYSTAL STRUCTURE CONSULTING

P.O. BOX 82266 • LINCOLN, NEBRASKA 68501
TELEPHONE (402) 421-2797

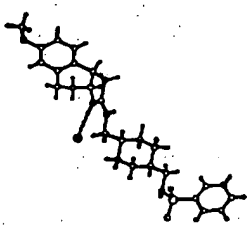
Exhibit G

BRIEF EXPERIMENTAL DESCRIPTION TO BE INCLUDED IN TEXT OR AS A FOOTNOTE AT TIME OF PUBLICATION

Single crystals of $[C_{27}H_{36}N_3O_3S][Cl]$ are, at 20±1°C, orthorhombic, space group $Pna2_1$ - C_{2v}^9 (No. 33) with $\underline{a}$ = 42.245(1) Å, $\underline{b}$ = 5.3262(2) Å, $\underline{c}$ = 11.9748(4) Å, V = 2694.4(2) Å^3, and Z = 4 {d_{calcd} = 1.277 gcm^{-3}; μ_a(CuK$\bar{\alpha}$) = 2.24 mm^{-1}}. A full hemisphere of diffracted intensities (omega or phi scans with width of 0.25°) was measured using graphite-monochromated CuKα radiation on a Siemens X-1000 HI-STAR Multiwire area detector. X-rays were provided by a Siemens M18XHF rotating anode operated at 40kV and 70mA. The sample was a nonmerohedrally twinned specimen containing two domains; the major domain had approximately 17 times the volume of the minor domain and only 4% of the reflections for the two domains were partially overlapped. There were no totally overlapping reflections and partially overlapping reflections were not used for structure refinement. The diffraction data from each domain was used to solve the structure independently and both gave the same species. The results reported herein are for the major domain but nearly identical structural parameters resulted from refinement using the nonoverlapping data for both domains simultaneously. Structure refinement using just the data from the minor domain gave structural parameters with reduced precision.

Lattice constants for the major domain were determined with the Siemens SAINT software package using peak centers for 2292 reflections. A total of 4902 integrated reflection intensities having 2θ(CuK$\bar{\alpha}$)< 104.3° were produced using the Siemens program SAINT. A total of 2788 of these were independent and gave R_{int} = 0.057. The Siemens SHELXTL-PC software package was used to solve the structure using "Direct Methods" techniques. All stages of weighted full-matrix least-squares refinement were conducted using F_o^2 data and the SHELXTL-PC Version 5 software package and converged to give R_1 (unweighted, based on F) = 0.053 for 2223 independent absorption-corrected reflections having 2θ(CuK$\bar{\alpha}$)< 104.3° and I>2σ(I) and w$\underline{R}_2$ (weighted, based on F^2) = 0.145 for 2673 independent absorption-corrected reflections having 2θ(CuK$\bar{\alpha}$)< 104.3° and I>0. Final R values for all 2788 independent absorption-corrected reflections having 2θ(CuK$\bar{\alpha}$)< 104.3° are: R_1 (unweighted, based on F) = 0.074 and w$\underline{R}_2$ (weighted, based on F^2) = 0.166. The structural model incorporated anisotropic thermal parameters for all nonhydrogen

atoms and isotropic thermal parameters for all hydrogen atoms. Hydrogen atoms H_{1N}, H_{2N} and H_{3N} were located from a difference Fourier map and refined as independent isotropic atoms. The remaining hydrogen atoms were included in the structure factor calculations as idealized atoms (assuming sp^2- or sp^3-hybridization of the carbon atoms and C-H bond lengths of 0.93-0.98 Å) "riding" on their respective carbon atoms. The isotropic thermal parameters for H_{1N}, H_{2N} and H_{3N} refined to final U_{iso} values of 0.10(3), 0.11(3) and 0.01(2)$Å^2$, respectively. The isotropic thermal parameters of the remaining hydrogen atoms were fixed at values 1.2 (nonmethyl) or 1.5 (methyl) times the equivalent isotropic thermal parameters of the carbon atoms to which they are covalently bonded. The methyl group (C_{27} and its hydrogens) was refined as a rigid rotor (using idealized sp^3-hybridized geometry and a C-H bond length of 0.96 Å) with three rotational parameters in each least-squares cycle. The refined values of these rotational parameters gave O-C-H angles which ranged from 105° to 117°.



Crystalytics Company
Crystal Structure Analysis Report

Compound Formula: $[C_{27}H_{36}N_3O_3S][Cl]$ Reference Code: CFS4-0799

R. W. J. sample #14794-65-1 (Jim McNally)

Description of Single-Crystal Sample and Mounting Used for Data Collection:

1) Color: Colorless
2) Shape: Flat plate
3) Dimensions: 0.025 mm. x 0.125 mm. x 0.175 mm.
4) Indices of Faces:
5) Crystal Mount: Crystal was glued with epoxy to the end of a thin glass fiber.
6) Crystal Orientation: Crystal was oriented with its longest edge nearly parallel to the phi axis of the diffractometer.
7) Comments: Sample was recrystallized from methanol/ethylacetate solution.

Space Group and Cell Data:

1) Crystal System: Orthorhombic Space Group and Number[1]: $Pna2_1$ - C_{2v}^9 (No. 33)
2) Number of Computer-Centered Reflections Used in the Least-Squares Refinement of the Cell Dimensions: 2292 measured at: 20±2 °C
3) Lattice Constants with esd's:

a = 42.245(1) Å	α = 90.000°	V = 2694.4(2) Å^3
b = 5.3262(2) Å	β = 90.000°	Z = 4 formula units
c = 11.9748(4) Å	γ = 90.000°	λ = 1.54178 Å

4) Molecular Weight: 518.10 amu/formula unit Calculated Density: 1.277 g·cm^{-3}
5) Linear Absorption Coefficient[2a]: 2.24 mm^{-1} F(000) = 1104.
6) Comments: The sample was a nonmerohedrally twinned specimen containing two domains; the major domain had approximately 17 times the volume of the minor domain and only 4% of the reflections for the two domains were partially overlapped. There were no totally overlapping reflections and partially overlapping reflections were not used for structure refinement. The diffraction data from each domain was used to solve the structure independently and both gave the same species. The results reported herein are for the major domain but nearly identical structural parameters resulted from refinement using the nonoverlapping data for both domains simultaneously. Structure refinement using just the data from the minor domain gave structural parameters with reduced precision.

Description of Data Collection[3]:

1) Instrument: Bruker X-1000 HI-STAR Single Crystal Multiwire Diffraction System
2) X-ray Source: Bruker M18XHF Rotating Anode with 0.3 x 3.0 mm. filament
3) Radiation: CuKα Power: 40 kV 70 mA
4) X Monochromator: X Graphite ___Other (Specify:)
   ___Filter: ___Nickel ___Niobium ___Other (Specify:)
5) Incident Beam Collimator Diameter: 0.5 mm Temperature: 20±2 °C
6) Scan Axis: X Omega or X Phi
7) Scan Width: 0.25° 2θ Range of Data : 8.38° - 104.28°
8) Sample to Detector Distance: 8.56 cm
9) Portion of Ewald Sphere Collected: Hemisphere
10) Number of frames collected: 3228 Seconds/frame: 60
11) Total Number of Reflections Collected: 4902
12) Number of Independent Reflections Collected: 2788
13) Data Collected: $-28 \le h \le 43$; $-5 \le k \le 5$; $-11 \le l \le 12$ R_{int}[4] = 0.057

Data Reduction[3]:

1) Lorentz and Polarization Corrections? Yes
2) Absorption Correction: Yes Range of transmission factors: 0.524 - 0.666
   XX Empirical Correction using Measurements for Equivalent Reflections
   (508 Reflections used)
   ___ Face-Indexed Gaussian Grid Correction
3) Comments:

Structure Solution[5]:

1) Method(s) Used in Structure Solution
   ___Heavy-atom Patterson Techniques
   XX Direct Methods
      a) XX SHELXTL/PC
      b) ___Other
   ___Other Techniques
2) Hydrogen Atom Positions Located? Yes
   After Refinement Cycle # 2 by XX Difference Fourier
   XX Calculated
3) Comments:

Structure Refinement[5]: (see next page for summary of refinement cycles)

1) Final Scale Factor: 0.327(1)
2) Extinction Parameter[6] Refined? Yes Final Value: 0.0002(2)
   Form: $k[1+0.001(x)(F_c^2)(\lambda^3)/\sin(2\theta)]^{-1/4}$
3) Anomalous Dispersion Corrections[2b] for Which Atoms: Cl, S, O, N, C
4) Variable Occupancies for Which Atoms? None

Atom	Final Occupancy	Atomic Form Factor[2c] Used

5) Refinement Constraints/Restraints: Hydrogen atoms H_{1N}, H_{2N} and H_{3N} were located from a difference Fourier map and refined as independent isotropic atoms. The remaining hydrogen atoms were included in the structure factor calculations as idealized atoms (assuming sp^2- or sp^3-hybridization of the carbon atoms and C-H bond lengths of 0.93-0.98 Å) "riding" on their respective carbon atoms. The isotropic thermal parameters for H_{1N}, H_{2N} and H_{3N} refined to final U_{iso} values of 0.10(3), 0.11(3) and 0.01(2)Å^2, respectively. The isotropic thermal parameters of the remaining hydrogen atoms were fixed at values 1.2 (nonmethyl) or 1.5 (methyl) times the equivalent isotropic thermal parameters of the carbon atoms to which they are covalently bonded. The methyl group (C_{27} and its hydrogens) was refined as a rigid rotor (using idealized sp^3-hybridized geometry and a C-H bond length of 0.96 Å) with three rotational parameters in each least-squares cycle. The refined values of these rotational parameters gave O-C-H angles which ranged from 105° to 117°.

6) Shift/Error Analysis for Final Least-Squares Cycle[7]:
   Maximum Shift for all Parameters: 0.000 σ_p Mean Shift for all Parameters: 0.000 σ_p

7) Peaks found in Final Difference Fourier Map: There were no peaks present in the final difference Fourier map above the background level (0.35 e$^-$/Å^3). The minimum and mean electron density in the final difference Fourier were -0.19 and 0.00 e$^-$/Å^3, respectively. The rms deviation from the mean electron density was 0.04 e$^-$/Å^3.

Summary of Full Matrix Least-Squares Refinement[8] Cycles

Cycle Number	sin θ/λ Minimum	sin θ/λ Maximum	Anisotropic[9] Atoms Number and Type	Isotropic Atoms Number and Type	Isotropic Atoms Positions Refined	Isotropic Atoms Thermal Parameters	# Refined Parameters	R_1 (unweighted,based on F) R_1[11]	# Observed Reflections	$F_o/\sigma(F_o)$ Cutoff	R_2 (weighted,based on F^2)[10] R_2[12]	Total # Independent Reflections	'Goodness-of-fit' (Goof)[13]	Extinction Correction
1	0.00	0.51		27 C, 3 N 3 O, 1 S 1 Cl	X	X	141	0.093	2223	4.0	0.249	2673	1.755	
2	0.00	0.51	27 C, 3 N 3 O, 1 S 1 Cl				316	0.074	2223	4.0	0.193	2673	1.400	
3	0.00	0.51	27 C, 3 N 3 O, 1 S 1 Cl	*36H	X	X	332	0.053	2223	4.0	0.145	2673	1.045	X

* See Item 5 on page 3 regarding the treatment of the hydrogen atoms.

Final Statistics from Cycle #3 for All of the Reflection Data: R_1 = 0.074; wR_2 = 0.166; GOOF = 1.169 for 2788 reflections

The correctness of the assigned absolute configuration was checked using the "Flack" absolute structure parameter[14] which refined to a final value of 0.18(3).

Exhibit L

References and Notes

1. "International Tables for X-Ray Crystallography", Vol. A, Kluwer Academic Publishers, Dordrecht, 1995.

2. "International Tables for X-Ray Crystallography", Vol. C, Kluwer Academic Publishers, Dordrecht, 1992; a) Tables 4.2.4.2 pp. 193-199; b) Tables 4.2.6.8 pp 219-222; c) Tables 6.1.1.4 pp 500-502.

3. Data acquisition and reduction was accomplished using standard versions of Siemens/Bruker software for the diffraction system.

4. $R_{int} = \Sigma|F_o^2 - F_o^2(mean)| \; / \; \Sigma[F_o]^2$

5. All structure determination and refinement calculations were performed on an IBM compatible 486 or 586 personal computer using the Siemens/Bruker SHELXTL Version 5.0 PC interactive software package.

6. A. C. Larson in "Crystallographic Computing", 1970, Ed. F. R. Ahmed, Munksgaard, Copenhagen, pp 291-294.

7. σ_p is the estimated standard deviation of the parameter in question.

8. Refinement on F^2 for all reflections except for 115 with negative F^2. Weighted R-factors wR_2 and all goodnesses of fit S are based on F^2, conventional R-factors R_1 are based on F, with F set to zero for negative F^2. The observed criterion of $F^2 > 2\text{sigma}(F^2)$ is used only for calculating "R-factor obs" etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on all data will be even larger.

9. The anisotropic thermal parameter is of the form:
$\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$.

10. The weighting scheme used is defined as: $w = 1 / [\sigma^2(F_o^2) + (a^*P)^2 + b^*P + d + e^*\sin(\theta)]$ where $P = [F_o^2 + 2F_c^2]/3$. In this case, a= 0.0938, b= 0, d = 0 and e = 0.

11. $\underline{R}_1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$

12. $w\underline{R}_2 = [\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]]^{1/2}$

13. GooF = S = $[\Sigma[w(F_o^2-F_c^2)^2]/(n-p)]^{1/2}$ where n is the total number of reflections and p is the number of parameters refined.

14. The value of the "Flack absolute structure parameter", x, should be 0.00 for the correct enantiomorphic description and 1.00 for the inverted description: a) H. D. Flack, *Acta Cryst.*, 1983, *A39*, 876-881; b) G. Bernardinelli and H. D. Flack, *Acta Cryst.*, 1985, *A41*, 500-511.

Table 1. Atomic Coordinates for Nonhydrogen Atoms in Crystalline $[C_{27}H_{36}N_3O_3S][Cl]$ [a]

Atom Type[b]	Fractional Coordinates 10^4x	10^4y	10^4z	Equivalent Isotropic Thermal Parameter, U, $Å^2 \times 10^3$ [c]
		Cation		
S	1890(1)	-1817(3)	3378(2)	62(1)
O_1	1739(1)	-4228(8)	3392(5)	84(1)
O_2	2083(1)	-1058(9)	4292(4)	79(1)
O_3	-1850(1)	7660(12)	3106(5)	105(2)
N_1	-362(1)	2030(13)	2990(6)	62(2)
N_2	-53(1)	5255(12)	2246(6)	66(2)
N_3	1619(2)	209(16)	3278(7)	67(2)
C_1	-297(2)	3645(14)	2220(6)	59(2)
C_2	-525(2)	3482(13)	1278(5)	65(2)
C_3	-793(2)	1762(14)	1736(6)	67(2)
C_4	-1083(2)	3353(14)	2115(6)	64(2)
C_5	-1248(2)	4655(17)	1347(7)	86(2)
C_6	-1510(2)	6149(16)	1651(8)	87(3)
C_7	-1598(2)	6274(16)	2739(8)	77(2)
C_8	-1441(2)	4911(14)	3526(7)	73(2)
C_9	-1175(1)	3462(11)	3245(6)	55(2)
C_{10}	-996(2)	2072(16)	4119(6)	77(2)
C_{11}	-829(2)	-256(15)	3679(6)	75(2)
C_{12}	-629(2)	351(13)	2681(6)	61(2)
C_{13}	186(2)	5209(14)	3088(6)	66(2)
C_{14}	443(1)	3309(12)	2830(5)	53(2)
C_{15}	630(2)	4008(13)	1781(6)	62(2)
C_{16}	906(1)	2211(14)	1576(5)	60(2)
C_{17}	1121(1)	2009(12)	2563(5)	52(2)
C_{18}	931(1)	1224(13)	3608(5)	59(2)
C_{19}	663(2)	3025(14)	3812(5)	64(2)

Table 1. (continued)

Atom Type[b]	Fractional Coordinates 10^4x	10^4y	10^4z	Equivalent Isotropic Thermal Parameter, U, $Å^2 \times 10^3$ [c]
C_{20}	1388(1)	186(14)	2353(6)	63(2)
C_{21}	2110(2)	-1655(13)	2128(6)	60(2)
C_{22}	2064(2)	-3338(17)	1289(8)	94(3)
C_{23}	2237(2)	-3108(20)	305(9)	111(3)
C_{24}	2456(2)	-1242(21)	189(9)	105(3)
C_{25}	2502(2)	386(19)	1015(9)	102(3)
C_{26}	2332(2)	215(17)	1990(8)	90(3)
C_{27}	-1972(2)	9523(21)	2397(10)	122(4)
		Anion		
Cl	-64(1)	744(4)	5362(2)	75(1)

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit.
[b] Atoms are labeled in agreement with Figure 1.
[c] This is one-third of the trace of the orthogonalized U_{ij} tensor.

Table 2. Anisotropic Thermal Parameters for Nonhydrogen Atoms in Crystalline $[C_{27}H_{36}N_3O_3S][Cl]$ [a,b]

Atom Type[c]	Anisotropic Thermal Parameters ($Å^2 \times 10^3$) U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
			Cation			
S	59(1)	55(1)	74(1)	6(1)	-14(1)	-3(1)
O_1	82(3)	48(3)	121(4)	21(3)	-10(3)	-13(2)
O_2	81(3)	79(3)	77(3)	6(3)	-22(3)	-15(3)
O_3	79(3)	116(5)	120(6)	20(4)	21(4)	29(3)
N_1	58(4)	73(4)	56(4)	4(4)	0(3)	6(3)
N_2	56(4)	56(4)	86(5)	4(4)	8(3)	4(3)
N_3	68(4)	61(5)	73(5)	-11(5)	-12(3)	-17(4)
C_1	64(5)	69(5)	44(4)	13(4)	1(4)	22(4)
C_2	62(4)	74(5)	60(4)	4(4)	8(4)	16(4)
C_3	51(4)	71(5)	79(5)	-15(4)	15(4)	12(4)
C_4	61(4)	66(5)	66(5)	8(4)	-11(4)	-10(4)
C_5	78(5)	108(7)	74(5)	3(5)	-15(5)	18(5)
C_6	68(5)	96(7)	96(7)	27(5)	-10(5)	19(5)
C_7	41(4)	95(6)	95(6)	19(5)	0(4)	10(4)
C_8	60(4)	76(5)	84(5)	4(5)	7(4)	-8(4)
C_9	47(3)	57(4)	60(5)	9(4)	1(3)	1(3)
C_{10}	69(5)	91(6)	72(5)	10(5)	7(4)	-12(5)
C_{11}	67(4)	80(5)	77(5)	10(5)	-15(4)	-6(4)
C_{12}	56(4)	56(4)	72(5)	-5(4)	-3(4)	4(4)
C_{13}	55(4)	68(4)	75(5)	-6(4)	3(4)	2(3)
C_{14}	47(3)	52(4)	60(4)	2(3)	7(3)	7(3)
C_{15}	57(4)	60(4)	69(5)	2(4)	4(4)	3(4)
C_{16}	54(4)	67(5)	58(4)	-1(4)	9(3)	7(3)
C_{17}	50(4)	54(4)	52(4)	0(3)	4(3)	0(3)
C_{18}	52(4)	72(5)	53(4)	0(4)	0(3)	3(3)
C_{19}	66(4)	80(5)	47(4)	3(4)	6(3)	-13(4)
C_{20}	50(4)	69(5)	68(5)	-9(4)	-2(4)	7(4)

Table 2. (continued)

Atom Type[c]	Anisotropic Thermal Parameters ($Å^2 \times 10^3$) U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C_{21}	57(4)	47(4)	75(5)	3(4)	-1(4)	0(4)
C_{22}	84(6)	87(6)	109(7)	-34(6)	11(5)	-8(5)
C_{23}	105(7)	110(8)	118(8)	-33(7)	40(7)	0(6)
C_{24}	104(7)	104(7)	108(8)	-21(7)	27(6)	7(6)
C_{25}	96(6)	100(7)	109(8)	-7(7)	33(6)	-23(6)
C_{26}	92(6)	80(6)	99(7)	-12(5)	28(5)	-21(5)
C_{27}	97(7)	103(8)	164(11)	14(8)	-6(7)	33(6)
			Anion			
Cl	85(1)	75(1)	65(1)	11(1)	-10(1)	-1(1)

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit.
[b] The form of the anisotropic thermal parameter is: $\exp[-2\pi^2(U_{11}h^2a^{*2} + U_{22}k^2b^{*2} + U_{33}l^2c^{*2} + 2U_{12}hka^*b^* + 2U_{13}hla^*c^* + 2U_{23}klb^*c^*)]$.
[c] Atoms are labeled in agreement with Figure 1.

Table 3. Atomic Coordinates for Hydrogen Atoms in Crystalline $[C_{27}H_{36}N_3O_3S][Cl]$ [a]

Atom Type[b]	Fractional Coordinates 10^4x	10^4y	10^4z
H_{1N}[c]	-288(20)	1722(159)	3622(80)
H_{2N}[c]	1(18)	6723(161)	1614(80)
H_{3N}[c]	1657(12)	1194(90)	3415(53)
H_{2b}	-427	2747	623
H_{2c}	-607	5129	1086
H_3	-858	573	1155
H_5	-1187	4570	601
H_6	-1622	7037	1110
H_8	-1511	4938	4262
H_{10a}	-1141	1579	4707
H_{10b}	-839	3188	4445
H_{11a}	-696	-957	4263
H_{11b}	-985	-1509	3476
H_{12}	-542	-1217	2382
H_{13a}	89	4797	3800
H_{13b}	279	6865	3152
H_{14}	342	1683	2697
H_{15a}	490	3978	1140
H_{15b}	711	5703	1859
H_{16a}	824	561	1397
H_{16b}	1027	2795	938
H_{17}	1213	3668	2704
H_{18a}	847	-455	3504
H_{18b}	1070	1200	4253
H_{19a}	750	4658	3997
H_{19b}	542	2449	4450
H_{20a}	1302	-1493	2271
H_{20b}	1494	628	1662

Table 3. (continued)

Atom Type[b]	Fractional Coordinates 10^4x	10^4y	10^4z
H_{22}	1918	-4630	1371
H_{23}	2204	-4234	-276
H_{24}	2572	-1109	-467
H_{25}	2652	1655	931
H_{26}	2367	1368	2561
H_{27a}	-2103	10560	2860
H_{27b}	-1822	10551	2008
H_{27c}	-2101	8649	1868

a Hydrogen atoms covalently bonded to nitrogens (H_{1N}, H_{2N} and H_{3N}) were located from a difference Fourier map and refined as independent isotropic atoms. The remaining hydrogen atoms were included in the structure factor calculations as idealized atoms (assuming sp^2- or sp^3-hybridization of the carbon atoms and C-H bond lengths of 0.93 Å to 0.98 Å) "riding" on their respective carbon atoms. The methyl group (C_{27} and its hydrogens) was refined as a rigid rotor (using idealized sp^3-hybridized geometry and a C-H bond length of 0.96 Å) with three rotational parameters in each least-squares cycle. The refined values of these rotational parameters gave O-C-H angles which ranged from 105° to 117°. The isotropic thermal parameters for H_{1N}, H_{2N} and H_{3N} refined to final U_{iso} values of 0.10(3), 0.11(3) and 0.01(2) $Å^2$, respectively. The isotropic thermal parameters of the remaining hydrogen atoms were fixed at values 1.2 (nonmethyl) or 1.5 (methyl) times the equivalent isotropic thermal parameters of the carbon atoms to which they are covalently bonded.

b Hydrogen atoms which are covalently bonded to carbon are labeled with the same numerical subscript(s) as their carbon atoms with an additional literal subscript (a, b or c) where necessary to distinguish between hydrogens bonded to the same carbon atom. The amine hydrogen atoms are labeled H_{1N} and H_{2N} and the sulfonamide hydrogen atom is labeled H_{3N}.

c The numbers in parentheses are the estimated standard deviations in the last significant digit.

Table 4. Bond Lengths in Crystalline $[C_{27}H_{36}N_3O_3S][Cl]$ [a]

Type[b]	Length, Å	Type[b]	Length, Å
$S\text{-}O_1$	1.434(4)	$S\text{-}O_2$	1.423(5)
$S\text{-}N_3$	1.579(8)	$S\text{-}C_{21}$	1.763(7)
$O_3\text{-}C_7$	1.368(9)	$O_3\text{-}C_{27}$	1.404(11)
$N_1\text{-}C_1$	1.291(9)	$C_1\text{-}C_2$	1.487(9)
$N_2\text{-}C_1$	1.340(9)	$C_9\text{-}C_{10}$	1.489(10)
$N_1\text{-}C_{12}$	1.487(9)	$N_1\text{-}H_{1N}$	0.84(9)
$N_2\text{-}C_{13}$	1.425(9)	$N_2\text{-}H_{2N}$	1.11(9)
$N_3\text{-}C_{20}$	1.477(10)	$N_3\text{-}H_{3N}$	0.57(5)
$C_2\text{-}C_3$	1.555(9)	$C_4\text{-}C_5$	1.346(10)
$C_3\text{-}C_{12}$	1.525(10)	$C_4\text{-}C_9$	1.408(10)
$C_3\text{-}C_4$	1.557(10)	$C_5\text{-}C_6$	1.413(11)
$C_{10}\text{-}C_{11}$	1.520(10)	$C_6\text{-}C_7$	1.356(12)
$C_{11}\text{-}C_{12}$	1.498(10)	$C_7\text{-}C_8$	1.362(10)
$C_{13}\text{-}C_{14}$	1.517(9)	$C_8\text{-}C_9$	1.406(9)
$C_{14}\text{-}C_{19}$	1.505(9)	$C_{21}\text{-}C_{22}$	1.361(10)
$C_{14}\text{-}C_{15}$	1.531(9)	$C_{21}\text{-}C_{26}$	1.377(10)
$C_{15}\text{-}C_{16}$	1.529(9)	$C_{22}\text{-}C_{23}$	1.392(13)
$C_{16}\text{-}C_{17}$	1.493(9)	$C_{23}\text{-}C_{24}$	1.364(13)
$C_{17}\text{-}C_{20}$	1.509(9)	$C_{24}\text{-}C_{25}$	1.329(12)
$C_{17}\text{-}C_{18}$	1.544(9)	$C_{25}\text{-}C_{26}$	1.375(12)
$C_{18}\text{-}C_{19}$	1.504(9)		

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit.

[b] Atoms are labeled in agreement with Figure 1.

Table 5. Bond Angles in Crystalline $[C_{27}H_{36}N_3O_3S][Cl]$ [a]

Type[b]	Angle, (deg)	Type[b]	Angle, (deg)
O_2SO_1	120.0(3)	O_2SC_{21}	109.8(3)
O_2SN_3	106.2(4)	O_1SC_{21}	106.8(4)
O_1SN_3	106.8(3)	N_3SC_{21}	106.5(4)
$C_7O_3C_{27}$	118.2(7)	$C_1N_2C_{13}$	123.2(7)
		$C_{20}N_3S$	122.1(6)
$C_1N_1C_{12}$	112.7(7)		
$C_1N_1H_{1N}$	134(6)	$C_{13}N_2H_{2N}$	111(4)
$C_{12}N_1H_{1N}$	113(6)	$C_{20}N_3H_{3N}$	114(6)
$C_1N_2H_{2N}$	126(4)	SN_3H_{3N}	114(6)
$N_1C_1N_2$	125.0(7)	$N_1C_1C_2$	111.4(7)
$N_2C_1C_2$	123.6(6)		
$C_1C_2C_3$	103.8(6)	$C_{19}C_{14}C_{15}$	110.3(5)
$C_{12}C_3C_2$	102.9(5)	$C_{13}C_{14}C_{15}$	112.0(5)
$C_{12}C_3C_4$	114.1(6)	$C_{16}C_{15}C_{14}$	112.0(5)
$C_2C_3C_4$	110.7(6)	$C_{17}C_{16}C_{15}$	112.4(5)
$C_9C_{10}C_{11}$	113.4(6)	$C_{16}C_{17}C_{20}$	111.6(5)
$C_{12}C_{11}C_{10}$	111.2(6)	$C_{16}C_{17}C_{18}$	110.3(5)
$N_1C_{12}C_{11}$	111.1(6)	$C_{20}C_{17}C_{18}$	110.4(5)
$N_1C_{12}C_3$	103.4(6)	$C_{19}C_{18}C_{17}$	110.5(5)
$C_{11}C_{12}C_3$	116.3(5)	$C_{18}C_{19}C_{14}$	113.7(5)
$N_2C_{13}C_{14}$	112.0(6)	$N_3C_{20}C_{17}$	111.4(6)
$C_{19}C_{14}C_{13}$	110.5(5)		
$C_5C_4C_9$	119.5(7)	$C_8C_9C_{10}$	120.8(7)

Table 5. (continued)

Type[b]	Angle, (deg)	Type[b]	Angle, (deg)
$C_5C_4C_3$	119.2(7)	$C_4C_9C_{10}$	121.0(6)
$C_9C_4C_3$	121.3(6)	$C_{22}C_{21}C_{26}$	119.0(7)
$C_4C_5C_6$	121.4(8)	$C_{22}C_{21}S$	121.3(6)
$C_7C_6C_5$	119.3(7)	$C_{26}C_{21}S$	119.7(6)
$C_6C_7C_8$	120.4(7)	$C_{21}C_{22}C_{23}$	119.5(8)
$C_6C_7O_3$	123.2(8)	$C_{24}C_{23}C_{22}$	120.4(10)
$C_8C_7O_3$	116.3(8)	$C_{25}C_{24}C_{23}$	120.0(9)
$C_7C_8C_9$	121.1(8)	$C_{24}C_{25}C_{26}$	120.7(9)
$C_8C_9C_4$	118.3(6)	$C_{25}C_{26}C_{21}$	120.4(9)

[a] The numbers in parentheses are the estimated standard deviations in the last significant digit.
[b] Atoms are labeled in agreement with Figure 1.

Table 6. Hydrogen-Bonding Interactions in Crystalline $[C_{27}H_{36}N_3O_3S][Cl]$

Donor Atom (D)[a]	Acceptor Atom (A)	Distance Å D···A	Distance Å H···A	Angle deg. D-H···A	Angle deg. H-D···A	Angle deg. H···A-X[b]	Asymmetric Unit of A[c]
N_1-H_{1N}	Cl	3.183	2.35	178	2	124(H_{2N})	x, y, z
N_2-H_{2N}	Cl	3.142	2.03	174	4	124(H_{1N})	-x, 1-y, -0.5+z
N_3-H_{3N}	O_1	3.009	2.46	161	16	162(S)	x, 1+y, z

a The hydrogen atom involved in the interaction is also indicated.

b The symbol X is used to denote the atoms which are covalently or hydrogen bonded to the acceptor atoms.

c All donor atoms belong to the asymmetric unit for which fractional atomic coordinates are given in Tables 1 and 3.

FIGURE CAPTIONS

Figure 1a. shows a perspective drawing of the solid-state structure for the HCl salt of $[C_{27}H_{35}N_3O_3S]$. Nonhydrogen atoms are represented by 50% probability thermal vibration ellipsoids and hydrogen atoms are represented by arbitrarily-small spheres which are in no way representative of their true thermal motion. The hydrogen-bonding interaction between the Cl^- anion and the hydrogen on amine nitrogen N_1 is shown with a dashed line.

Figure 1b. shows a perspective drawing of the solid-state structure for the HCl salt of $[C_{27}H_{35}N_3O_3S]$. The view is the same as in Figure 1a but the chlorine atom is now represented as a large dotted sphere, oxygen and nitrogen atoms are now represented by medium-sized shaded spheres, and sulfur, carbon and hydrogen atoms are represented by large, medium and small open spheres, respectively. The hydrogen-bonding interaction between the Cl^- anion and the hydrogen on amine nitrogen N_1 is shown with a dashed line.

Figure 1c. shows a perspective drawing of the structure for the $[C_{27}H_{36}N_3O_3S]^+$ cation, as observed in the solid-state structure of its Cl^- salt. Nonhydrogen atoms are represented by 50% probability thermal vibration ellipsoids and hydrogen atoms are represented by arbitrarily-small spheres which are in no way representative of their true thermal motion.

Figure 1d. shows a perspective drawing of the structure for the $[C_{27}H_{36}N_3O_3S]^+$ cation, as observed in the solid-state structure of its Cl^- salt. The view is the same as in Figure 1c but the oxygen and nitrogen atoms are now represented by medium-sized shaded spheres, and sulfur, carbon and hydrogen atoms are represented by large, medium and small open spheres, respectively.

Figure 1e. shows a space-filling drawing of the structure for the $[C_{27}H_{36}N_3O_3S]^+$ cation, as observed in the solid-state structure of its Cl^- salt. The view is as in Figure 1c.

Figure 1f. shows a perspective drawing of the hydrogen-bonding interaction involving the Cl^- anion and the amine (N_1 and N_2) nitrogens of two symmetry-related $[C_{27}H_{36}N_3O_3S]^+$ cations in the crystal. Atoms of the cation related by symmetry operation -x, 1-y, -0.5+z to the one shown in Figure 1d are labeled with a prime (′). Atoms are represented as in Figure 1b and the hydrogen bonds between the Cl^- anion and the $[C_{27}H_{36}N_3O_3S]^+$ cations are shown with dashed lines.

Figure 1g. shows a perspective drawing of the hydrogen-bonding interaction involving sufonamide proton H_{3N} and the sulfonamide oxygen atom of a symmetry-related $[C_{27}H_{36}N_3O_3S]^+$ cation in crystals of $[C_{27}H_{36}N_3O_3S][Cl]$. Atoms of the $[C_{27}H_{36}N_3O_3S]^+$ cation related by symmetry operation x, 1+y, z to the one shown in Figure 1d are labeled with double primes (″). Atoms are represented as in Figure 1b and the hydrogen bond between $[C_{27}H_{36}N_3O_3S]^+$ cations is shown with a dashed line as are the hydrogen bonds between the cation and Cl^- anion within each of the two asymmetric units shown.

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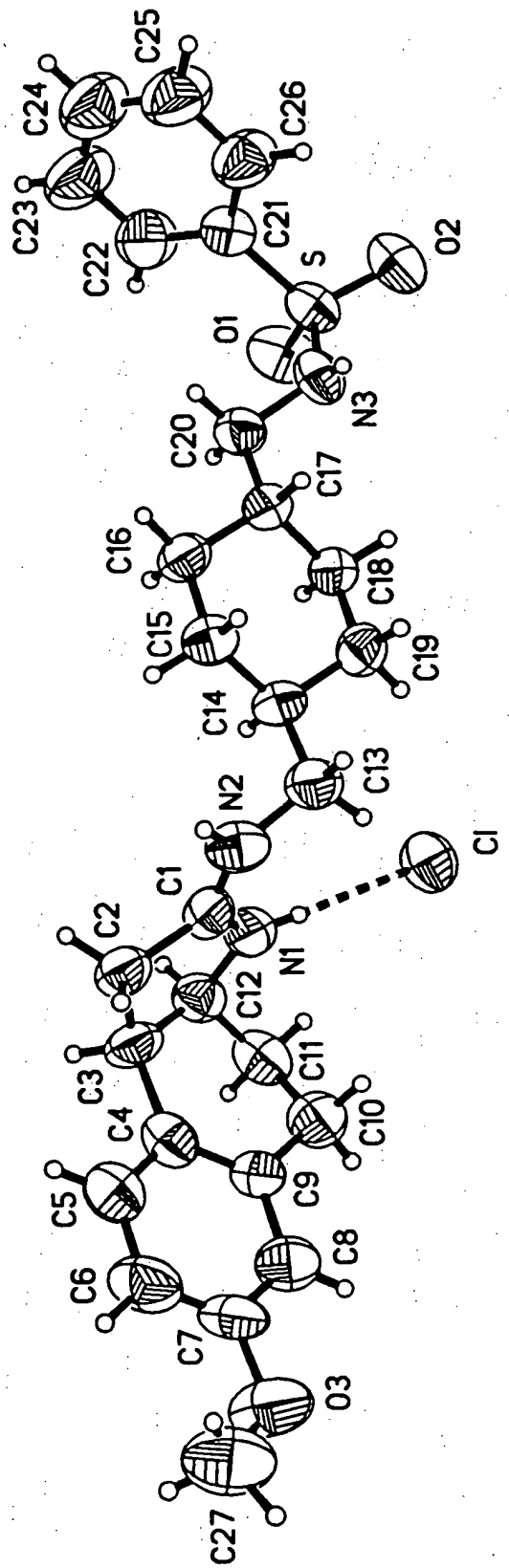
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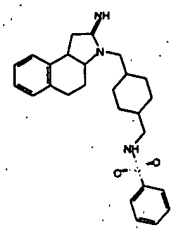
Exhibit AB



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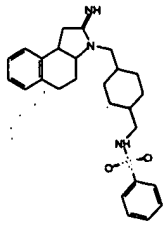

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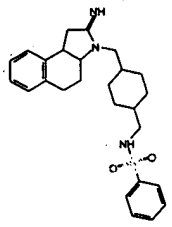

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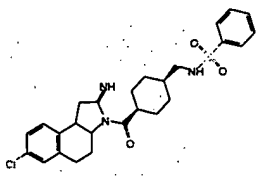

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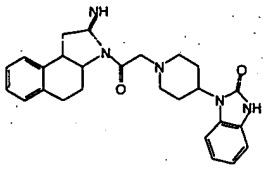

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page 145
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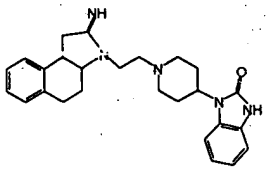
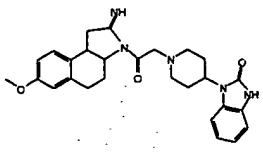
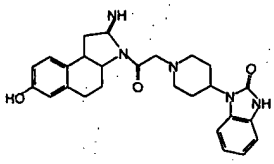


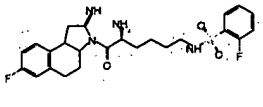
JNJ 7572071
BID 4362288
salt AFP
NB 14794
page 147
1



JNJ 8283535
BID 4730292
salt AAC
NB 14794
page 130
1



JNJ 8283626
BID 4730334
salt AAC
NB 14794
page 131
1



JNJ 8487960
BID 4832499
salt AAC
NB 14811
page 138
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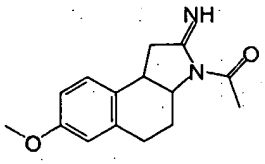
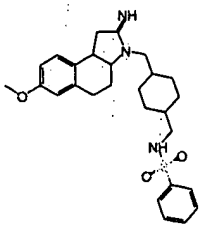
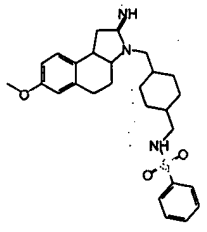


JNJ 8512335
BID 4844686
salt AAC
NB 14794
page 135
1



JNJ 8702460
BID 5213677
salt AAA
NB 17472
page 2
BGW



JNJ 8702460
BID 9713956
salt AAC
NB 8902
page 946
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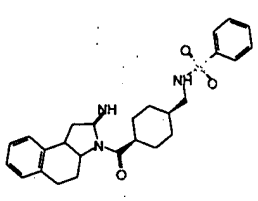
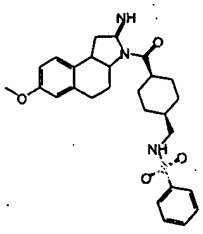
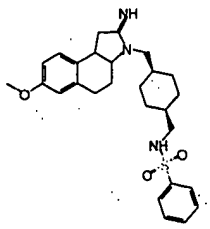


JNJ 17225728
BID 9890034
salt AAA
NB 14794
page 57
1

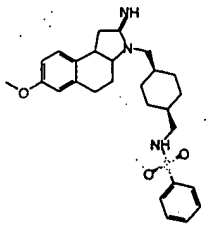


JNJ 17225767
BID 9890048
salt AAA
NB 14794
page 62
1

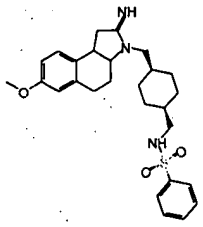
Exhibit AC



JNJ 17225858
BID 9890097
salt AAC
NB 14794
page 65
1



JNJ 17225858
BID 9943472
salt AAC
NB 14794
page 87
1



JNJ 17225858
BID 9943717
salt AAC
NB 14794
page 150
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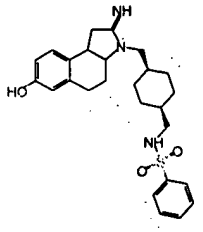

JNJ 17225884
BID 9890104
salt AAC
NB 14794
page 70
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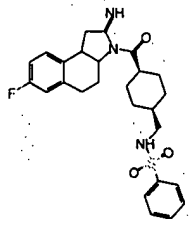
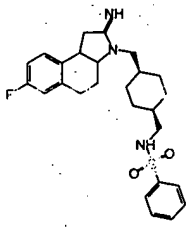
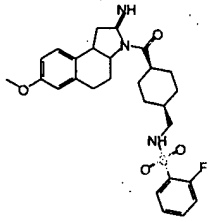


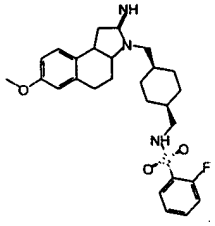
JNJ 17228107
BID 9891224
salt AAA
NB 14794
page 75
2



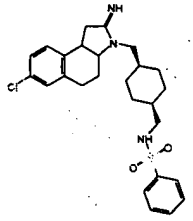
JNJ 17228276
BID 9891308
salt AAC
NB 14794
page 84
1



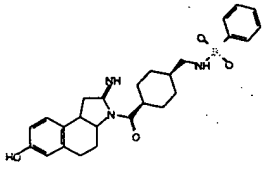
JNJ 17231019
BID 9892680
salt AFP
NB 14794
page 143
1



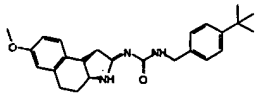
JNJ 17231318
BID 9892827
salt AFP
NB 14794
page 151
1



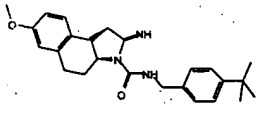
JNJ 17825522
BID 10358124
salt AAC
NB 14794
page 99
1



JNJ 17825548
BID 10358131
salt AAC
NB 14794
page 100
1



JNJ 17988906
BID 10448627
salt AFP
NB 17182
page 124
2



JNJ 17988919
BID 10448634
salt AFP
NB 17182
page 124
1

Exhibit AD

No. 14280-129

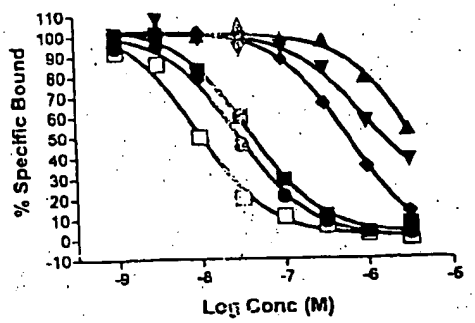
Project No. NPY5 Protocol / Experiment No. 308 Date

Subject Purpose

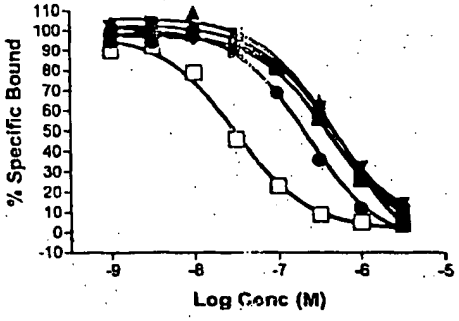
Contd. from page

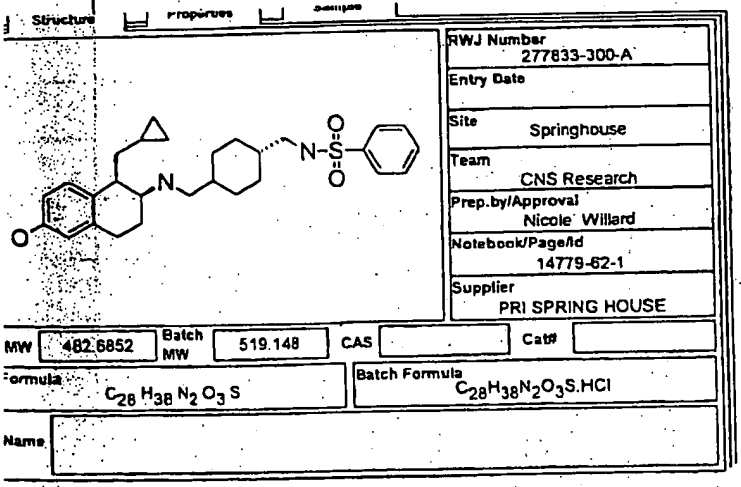
REAL NUMBER	Properties	NPY5 IC50 nM
277824-300-A	Y5	38
277825-300-A	Y5	3000
277826-300-A	Y5	1100
277827-300-A	Y5	621
277833-300-A	Y5	29
277802-300-A	Y5	422
[illegible]	Y5	417
[illegible]	Y5	437
057926-300-C	OB/OB	
058532-300-A	OB/OB	
058746-300-A	Y2,Y1	
058747-300-A	Y2	
058748-300-A	Y2	
058749-300-A	Y2	
275087-300-A	Y2	
277829-300-A	Y2	
58260-300-A	CONTROL	9
58442-300-A	CONTROL	31
58660-300-A	REPEAT	661
58691-300-A	REPEAT	225

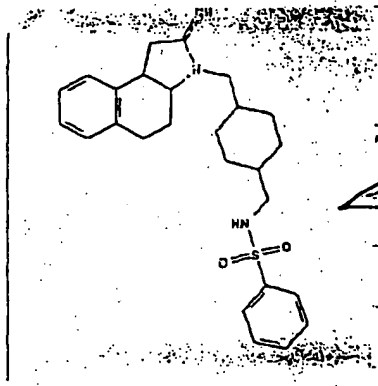
Binding of new RWJ compounds to recombinant human NPY5 receptor



Binding of new RWJ compounds to recombinant human NPY5 receptor







Could be very interesting

Jim must confirm structure

Contd. on page Investigator Date

Read and Understood Date

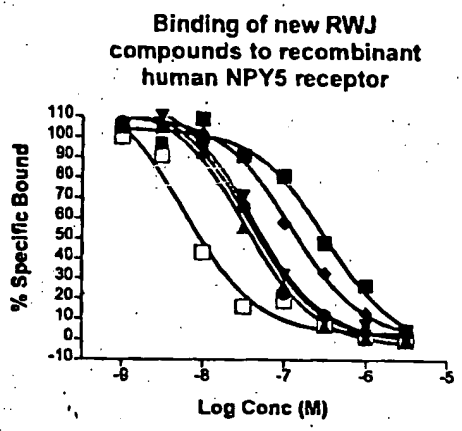
Exhibit AE

No. 14280-133

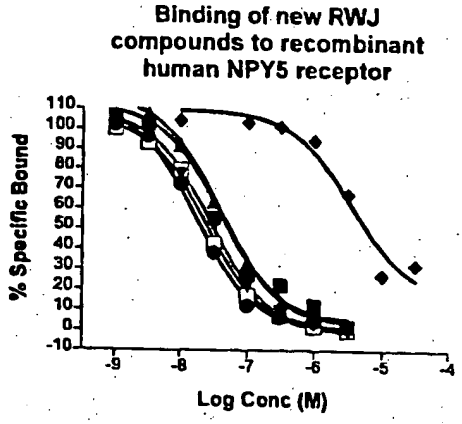
Project No. NPY5 Protocol / Experiment No. 311 Date

Subject Purpose

Contd. from page



REAL NUMBER	NPY5 IC50 nM
289060-300-A	324
289062-300-A	33
289136-300-A	40
289137-300-A	123
279518-300-A	37
279527-300-A	38
058532-300-A	
279527-300-A	
277824-300-B	26
277824-300-A	40
058260-300-A	6
058442-300-A	23
058669-300-A	17



Contd. on page Investigator Date

Read and Understood Date

Exhibit AF

No. 14280-147

Project No. NYY5 Protocol / Experiment No. 325 Date

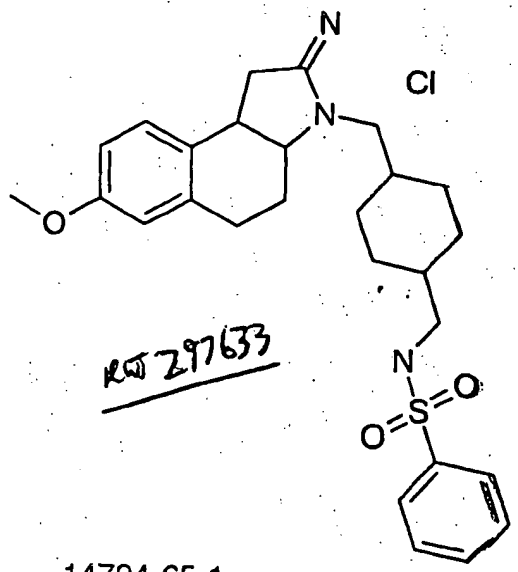
Subject Purpose

Contd. from page

Data 1	Data2	Data3		Average	Specific	%Specific	%Inhibition
1772.6	1866.3		297521	1819	19	0	100
2072.1	2159.4			2116	316	5	95
2852.5	3285.6			3069	1269	20	80
3838.7	3889.2			3864	2064	33	67
5800	6117.2			5959	4159	67	33
7512.8	7430.1			7471	5671	91	9
7163	7681.6			7422	5622	91	9
7749.2	8067.8			7909	6109	99	1
1890.4	1784.1		297561	1837	37	1	99
2218.7	2058.1			2138	338	5	95
2844.8	2981.9			2913	1113	18	82
4829.7	4741.9			4786	2986	48	52
6403.6	6567.5			6486	4686	76	24
7598.6	7494.5			7547	5747	93	7
7494.8	7733.1			7614	5814	94	6
7619.7	7641.2			7580	5780	93	7
2017.6	1777.3		297633	1897	97	2	98
2262.4	2151.4			2207	407	7	93
2140.9	2121.3			2131	331	5	95
2161.2	2249			2205	405	7	93
2539.5	2250.7			2395	595	10	90
2946.8	2914			2930	1130	18	82
4846.8	4301.6			4574	2774	45	55
6667.6	6814.3			6741	4941	80	20
2047.1	1892.8		297679	1970	170	3	97
2238.9	2306.5			2273	473	8	92
3152.7	3632.1			3392	1592	26	74
5382.4	5383.6			5383	3583	58	42
6760.8	7085.7			6923	5123	83	17
8191.5	7565			7878	6078	98	2
7929.7	8018.8			7974	6174	100	0
7400.3	7230.7			7316	5516	89	11
1752.5	1832.5		58260	1793	-8	0	100
2082.8	2221.3			2152	352	6	94
2100.7	1872.1			1986	186	3	97
2215.8	2305.3			2261	461	7	93
2793.6	3076.5			2905	1105	18	82
4252.1	4926.2			4589	2789	45	55
6222.1	6468.7			6345	4545	73	27
7283.4	6737.6			7011	5211	84	16
5416.8	5552.1		WRY-amide	5486	3686	59	41
6808.6	6742.3			6775	4975	80	20
7899	7328.1			7613	5813	94	6
7896.1	7543.1			7720	5920	95	5
8291.8	7680.8			7986	6186	100	0
8337.7	7927.3			8133	6333	102	-2
8154.6	9083.6			8619	6819	110	-10
7268.4	7134.5		Control	7201	5401	87	13

REAL NUMBER	NPY5 IC50 nM
297521-300-A	62
297561-300-A	106
297633-300-A	2
297679-300-A	150
295986-300-A	39
293708-300-A	Inactive
293710-300-A	Inactive
296148-300-A	
058427-300-A	29
058427-300-C	35
293376-300-A	39
293407-300-A	73
293420-300-A	362
293377-300-A	50
303114-300-A	412
303115-300-A	15
058442-300-A	29
058260-300-A	8
WRY-amide	3400

These values were averaged, omitted, so the data should be



REG 297633

Came out at less than 2 nM.

14794-65-1
Molecular Weight = 518.12

Contd. on page Investigator Date

Read and Understood Date

Exhibit AG

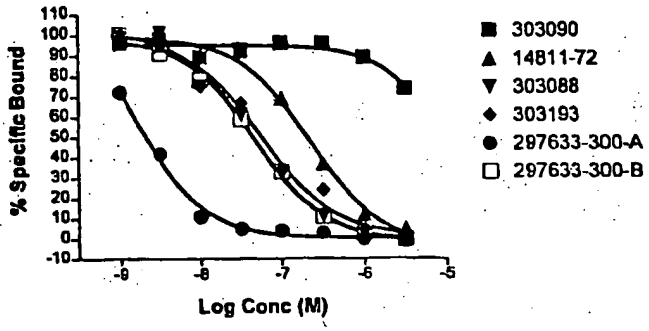
No. 14280-153

Project No. NPY5 Protocol / Experiment No. 323 Date

Subject Purpose

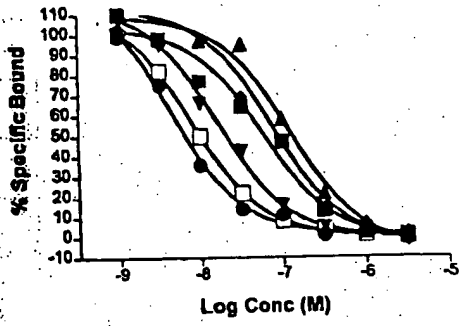
Contd. from page

Binding of new RWJ compounds to recombinant human NPY5 receptor



Compound	REAL NUMBER	NPY5 IC50 nM
14811-55	298270-300-A	Y2
14811-57	303090-300-A	Inactive
14811-72		227
14811-74	306450-300-A	Y2
14794-75-2	303088-300-A	44
14794-76-1	058260-300-C	8
14794-84-1	303193-300-A	58
14794-87-1	297633-300-B	47
	058260-300-C	Large Scale
	297633-300-B	Large Scale
REPEATS/ CONTROLS	297521-300-A	58
	297679-300-A	125
switch	297561-300-A	76
	058260-300-A	4
	058442-300-A	16
	297633-300-A	1.5

Binding of new RWJ c mpounds to recombinant human NPY5 receptor



It turns out I made mistake by switching caps.

297633 Was switched w/ 297679 so the 297633-300-B data is accurate

& 297633-300-A is actually 125 nM

297679-300-A is actually 1.5 nM

Contd. on page Investigator Date

Read and Understood Date

Exhibit AH

No. 14280-167

Project No. NPY5 Protocol / Experiment N . 735 Date

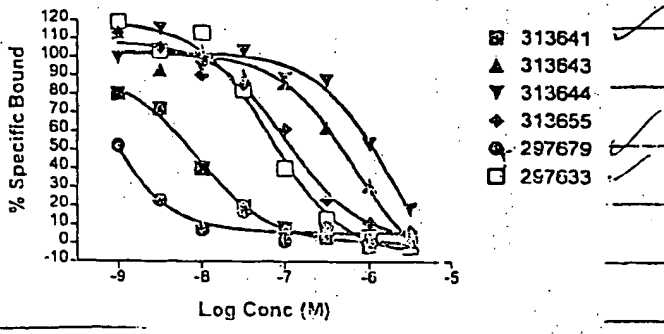
Subject Purpose

Contd. from page

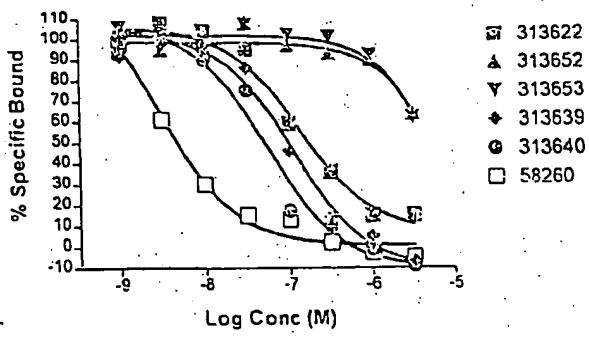
NUMBER	Properties	NPY5 IC50 nM	NPY2 IC50 nM
66-300-A	Y2		Inactive
13-300-A	Y2		Inactive**
99-300-A	Y2		3000
00-300-A	Y2		10000
22-300-A	Y5	133	
52-300-A	Y5	Inactive	
53-300-A	Y5	Inactive	
39-300-A	Y5	111	
40-300-A	Y5	54	
41-300-A	Y5	9	
43-300-A	Y5	647	
44-300-A	Y5	1000	
55-300-A	Y5	200	
60-300-A		3	
79-300-A		1	
88-300-A		67	
02-301-A			3000
71-301-A			3000
43-300-A	This is the cyclopropyl replaceme		4000

13 showed no dose response
overall lower amount of binding

Binding of new RWJ compounds to recombinant human NPY5 receptor



Binding of new RWJ compounds to recombinant human NPY5 receptor



Contd. on page Investigator Date

Read and Understood Date

Exhibit AI

No. 14280-175

Project No. NPY5 Protocol / Experiment No. 342 Date

Subject Purpose

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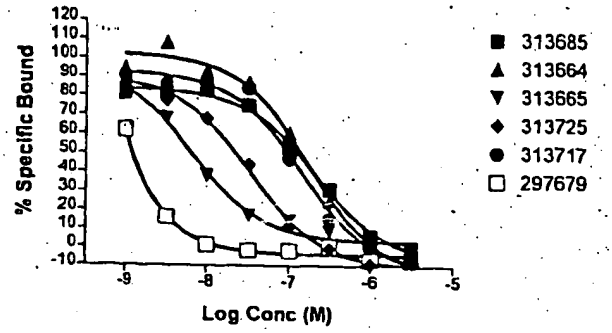
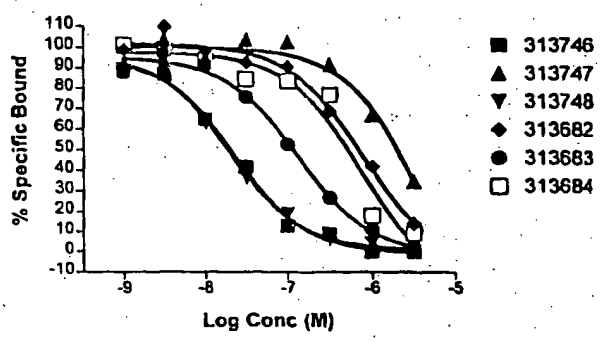
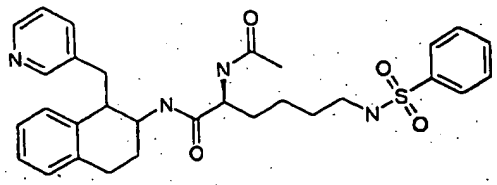


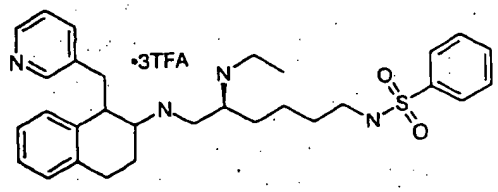


Compound	REAL NUMBER	NPY5 IC50 nM
14794-111-1	313746-300-A	23
14794-112-1	313747-300-A	2000
14794-113-1	313748-300-A	20
14205-087A	313682-300-A	769
14205-087-B	313683-300-A	133
14205-086-A	313684-300-A	745
14205-086-B	313685-300-A	200
14811-101	313664-300-A	200
14811-103	313665-300-A	7
14811-106	313725-300-A	33
14811-107-1	313717-300-A	142
Control	297679-300-A	1



14811-103
RWJ 313665-300-A

Here is another one:



14811-106
RWJ 313725-300-A

Removal of cyclopropyl sulfoN did not hurt activity when replaced with amide

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Read and Understood Date

Exhibit AJ

No. 14280-183

Project No. NPY5 Protocol / Experiment No. 349 Date

Subject Purpose

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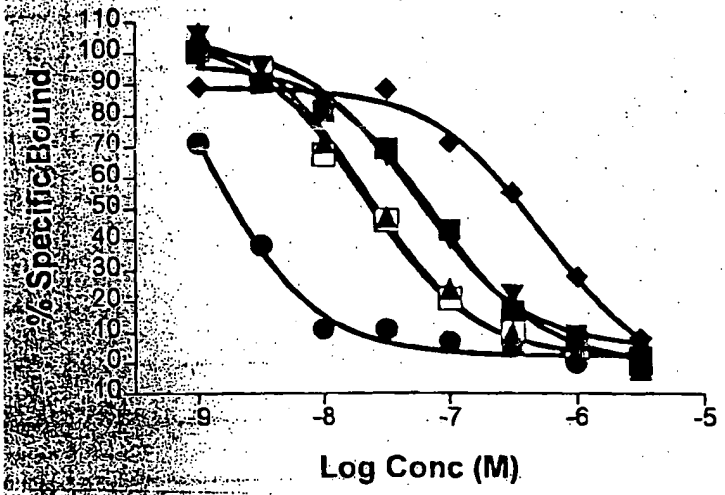
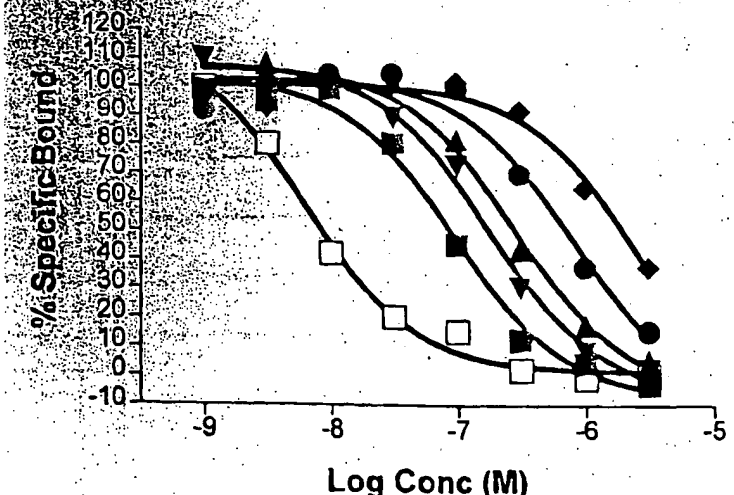
Binding of new RWJ compounds to recombinant human NPY5 receptor



	IC50
313725	96
313717	286
314246	175
314247	2500
314463	807
58260	6
314465	75
314466	23
314467	54
314464	548
297679	1
58442	22

Binding of new RWJ compounds to recombinant human NPY5 receptor



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Read and Understood Date

Exhibit AK

No. 14280-187

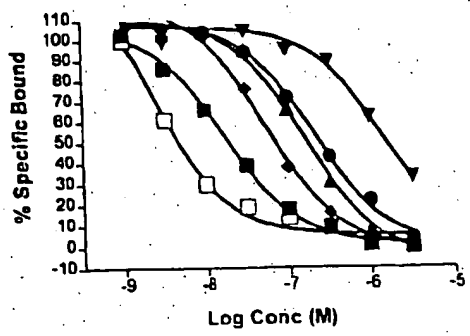
Project No. NPY5 Protocol / Experiment No. 351 Date

Subject Purpose

Contd. from page

Data 1	Data2	Data3		Average	Specific	%Specific	%Inhibition
1710.6	1690.9		313665	1711	-10	0	100
1728.6	1796.3			1763	41	1	99
2000.5	2497.4			2249	528	9	91
2742.8	2744.2			2744	1022	18	82
3990.1	3850.5			3920	2199	39	61
5146.5	5760.6			5454	3732	66	34
6762.2	6308.8			6536	4814	86	14
7505	7525.8			7515	5794	103	-3
1882.3	1913.9		314246	1898	177	3	97
2035.5	2313.7			2175	453	8	92
3535.9	3335.2			3436	1714	31	69
5712.5	5090.1			5401	3680	66	34
6807.5	7315.8			7062	5340	95	5
7195.1	7967.3			7581	5860	104	-4
7219.6	7832.4			7526	5805	103	-3
7844.8	8201.4			8023	6302	112	-12
3708.5	3404.6		314247	3555	1834	33	67
5256.9	5099.2			5178	3457	62	38
6904	6586.6			6745	5024	89	11
6042.5	8084.2			7063	5342	95	5
7764.1	7409.5			7586	5865	104	-4
6366.4	7608.5			7987	6266	112	-12
7367.8	7202.5			7285	5564	99	1
7768.7	8088.2			7928	6207	111	-11
1682	1953.5		313725	1818	97	2	98
1883.9	1989.6			1987	265	5	95
2491.4	2742.3			2617	896	16	84
3935.4	3815.9			3876	2154	38	62
6172.9	5789.1			5981	4260	76	24
7587.6	7311.9			7440	5719	102	-2
7445.1	7746.6			7596	5875	105	-5
8394.6				8395	6673	119	-19
2013.5	1917.6		313717	1965	244	4	96
2672.5	3248.2			2960	1239	22	78
4248.7	4076.5			4162	2440	43	57
5751.1	5745.9			5749	4027	72	28
6869.2	7102.1			6986	5264	94	6
7480.5	7683.5			7582	5861	104	-4
7240.7	8086.7			7664	5943	106	-6
7941.2	7990.5			7966	6245	111	-11
1671.6	1770.8		58260	1721	0	0	100
1886	1681.1			1784	62	1	99
2076.7	2341.8			2209	488	9	91
2690.3	2144.6			2517	796	14	86
2884.4	2708.1			2796	1075	19	81
3455.5	3402.1			3429	1708	30	70
5312.5	4871.2			5142	3421	61	39
7279	7394.3		Control	7337	5615	100	0

Data 1	Data2	Data3		Average	Specific	%Specific	%Inhibition
2456.6	2430.7		314704	2444	544	11	89
2739.4	2900.1			2820	920	18	82
4278.8	4366.8			4323	2423	48	52
5951.1	6528.8			6240	4340	85	15
6717.5	7331.8			7025	5125	100	0
6924.7	7385.2			7155	5255	103	-3
6572.3	6949.6			6761	4861	95	5
7262.5	7476.5			7370	5470	107	-7
1937.2	1741.6		316980	1839	-61	-1	101
2685.5	2620.7			2653	753	15	85
3695.3	3290.6			3493	1593	31	69
5036.2	5036.8			5037	3137	62	39
6449.1	6633.5			6541	4841	91	9
7041.7	7184.3			7113	5213	102	-2
	7594.3			7594	5694	112	-12
7424.7	7584.5			7505	5605	110	-10
4451.5	4468.6		317050	4460	2560	50	50
5900.7	6485.8			6193	4293	84	16
7050.1	7051.4			7051	5151	101	-1
7207.2	8055.1			7631	5731	112	-12
7538.5	7933.9			7736	5836	114	-14
7205.9	7553.6			7380	5480	107	-7
6998.1	7893.8			7446	5546	109	-9
7424.8	7996.7			7711	5811	114	-14
2954.4	3050		317051	3002	1102	22	78
4380	4226.5			4303	2403	47	53
6070.8	5922			5996	4096	80	20
8136.1	7411			7774	5874	115	-15
8038.8	7825.4			7932	6032	118	-18
7312.3	7286.3			7299	5399	106	-6
7481.5	7281.5			7382	5482	107	-7
7261.6	7254.6			7258	5358	105	-5
1797.9	1996.7		314503	1897	-3	0	100
1959.9	2263			2111	211	4	96
2461.5	2471			2466	566	11	89
3870.7	3731			3801	1901	37	63
5563.8	5263.4			5414	3514	69	31
6611.4	6575.5			6593	4693	92	8
6761.6	6793			6777	4877	96	4
7257	7072.9			7165	5265	103	-3
1948.2	1781.9		314709	1865	-35	-1	101
2329.3	2353.7			2342	442	9	91
2701.3	2585.5			2643	743	15	85
3866.2	3959.8			3913	2013	39	61
5614	5543.3			5579	3679	72	28
7131.5	6330.6			6731	4831	95	5
7147.7	8214.3			7681	5781	113	-13
7019.4	7358.9		Control	7189	5289	104	-4



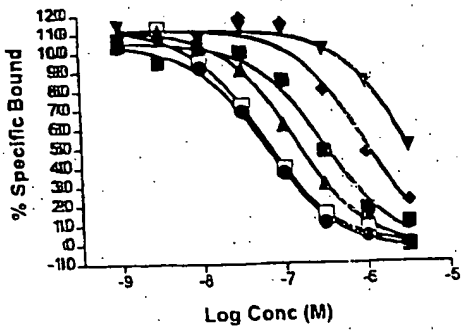


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Exhibit AL

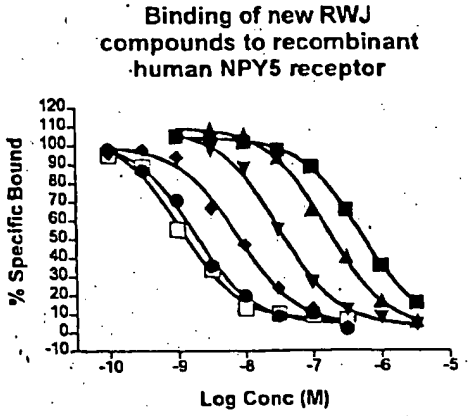
No. 14280-192

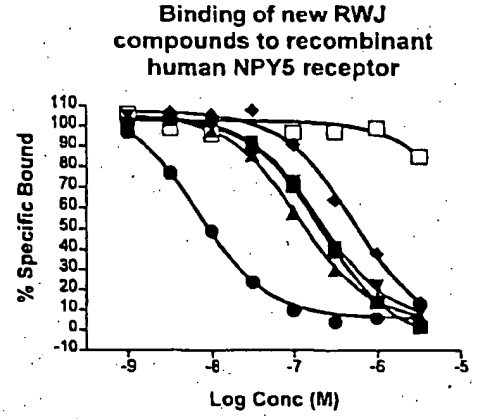
Project No. NPY5 Protocol / Experiment No. 357 Date

Subject Purpose

Contd. from page

REAL NUMBER	NPY5 IC50 nM
320563-300-A	32
320564-300-A	8
320566-300-A	Inactive
320605-300-A	878
318251-300-A	117
318252-300-A	539
320112-300-A	202
057836-300-A	222
318245-300-A	530
316035-300-A	168
314996-300-A	8
297679-300-A	1.7
314995-300-A	1





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Read and Understood Date

Exhibit AM

No. 15229- 21

Project No. NPY5 Protocol / Experiment No. 369 Date

Subject Purpose

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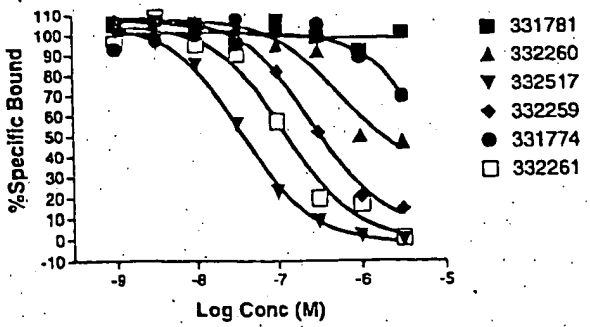
Data 1	Data2	Data3		Average	Specific	%Specific	%Inhibition
7271.3	7423.3		331781	7347	5737	131	-31
5374.9	5799.9			5587	3977	91	9
5953.6	5857.9			5906	4296	98	2
5878.1	6608.2			6243	4633	106	-6
5701.8	5824.3			5763	4153	95	5
6088.1	6384			6236	4626	105	-5
6240	6356.7			6298	4688	107	-7
6526.3	6016.1			6271	4661	106	-6
3694.8	3622.7		332260	3659	2049	47	53
2998	4601.5			3800	2190	50	50
5252.6	6001			5627	4017	91	9
5613	5870.8			5742	4132	94	6
5945.7	5986.8			5966	4356	99	1
6164.7	6373.3			6269	4659	106	-6
6568.9	6653.7			6611	5001	114	-14
6316.8	6139.6			6228	4618	105	-5
1626.5	1590.9		332517	1609	-1	0	100
1768.1	1665.1			1717	107	2	98
2145.3	1894.5			2020	410	9	91
2659.2	2555.6			2607	997	23	77
4092.4	4004.6			4049	2439	56	44
5542.6	5123.9			5333	3723	85	15
5744.3	5893			5819	4209	96	4
6199.3	5989.4			6094	4484	102	-2
2067.4	2437.3		332259	2252	642	15	85
2395.7	2665.3			2531	921	21	79
3591.6	4169.9			3881	2271	52	48
5104.9	5220.7			5163	3553	81	19
5744.7	6313.6			6029	4419	101	-1
6673.9	5753			6213	4603	105	-5
6504.6	6073.6			6289	4679	107	-7
6315.8	6306.9			6311	4701	107	-7
4490.8	4745.9		331774	4618	3008	69	31
5330.2	5577.4			5454	3844	88	12
5932.1	6394.9			6164	4554	104	-4
5985	6198.6			6092	4482	102	-2
6143.8	6434.1			6289	4679	107	-7
6132.9	5790.3			5962	4352	99	1
6173.1	5604.6			5889	4279	97	3
5865.8	5541.5			5704	4094	93	7
1756.9	1514.9		332261	1636	26	1	99
2869.7	1848			2359	749	17	83
2341	2601.6			2471	861	20	80
4248.5	3953.2			4101	2491	57	43
5654.1	5470.7			5562	3952	90	10
5457.5	6063.7			5761	4151	95	5
6348.8	6425.1			6387	4777	109	-9
5996.3	5644.6			5820	4210	96	4

REAL NUMBER	NPY5 IC50 nM
332261-300-A	121
332259-300-A	263
332260-300-A	3000
331781-300-A	>3000
331774-300-A	>3000
331775-300-A	54
332285-300-A	>3000
332360-300-A	2000
332300-300-A	>3000
114102-301-B	Y2
332517-300-A	35
332516-300-A	Y2
332518-300-A	2000
328568-300-A	265
306468-300-A	250
313717-300-A	280
328577-300-A	856
313665-300-A	39
314613-300-A	240
306672-300-A	133

Numbers are a bit higher than normal.

Repeat



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Investigator Date

Read and Understood S Feeney Date

Exhibit AN

No. 15229- 29

Project No. NPY5 Protocol / Experiment No. 374 Date

Subject Purpose

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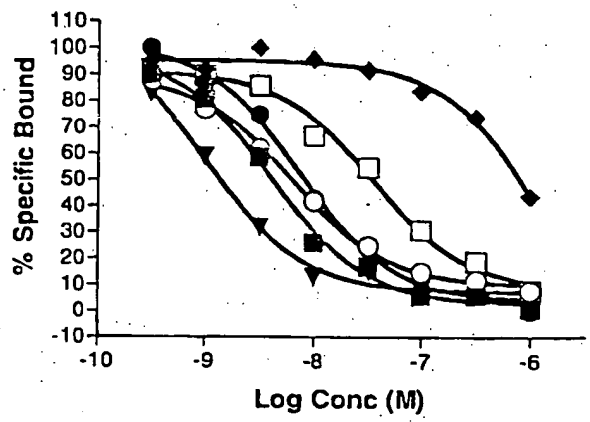
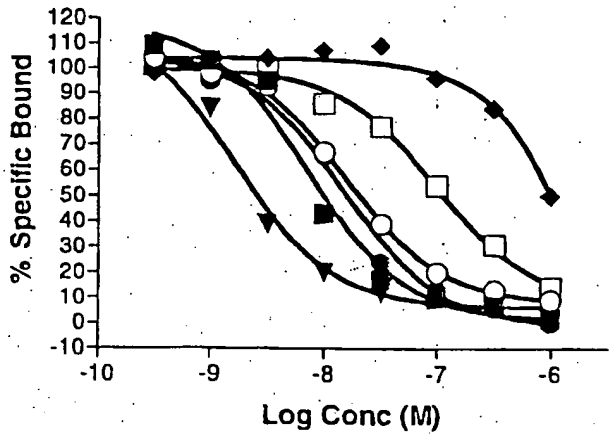
Binding of RWJ compounds to recombinant human NPY5 receptor



Binding affinities were similar for both rat + human receptor

Binding of RWJ compounds to recombinant rat NPY5 receptor



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Investigator S. Fawzi Date

Read and Understood Date

Exhibit AO

No. 15229- 47

Project No. NPY5 Protocol / Experiment No. 385 Date ...

Subject ..... Purpose .....

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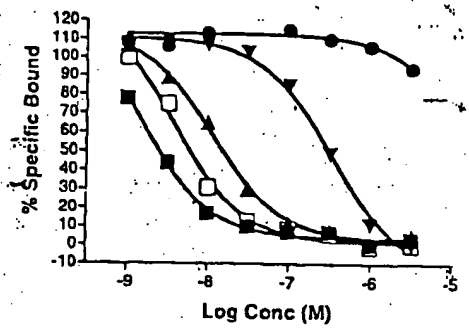

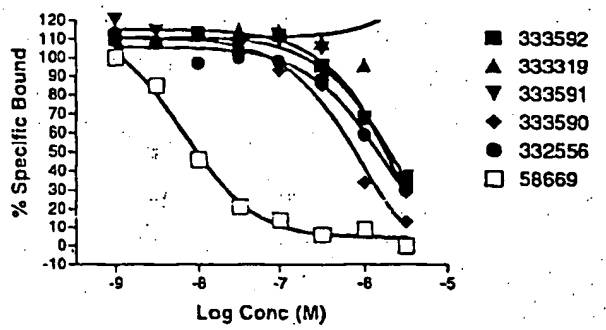

RWJ NUMBER	NPY5 IC50 nM
334170-300-A	335
333329-300-A	to be repeated
333328-300-A	Inactive
333592-300-A	2000
333319-300-A	Inactive
333591-300-A	2000
333590-300-A	836
058669-000-B	7
332556-300-A	1000
058442-002-A	
058669-300-D	
058442-300-A	11
297679-300-A	1.5
058260-300-A	4

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Read and Understood _____ Date _____

Exhibit AP

No. 15229- 46

Project No. MPY ..... Protocol / Experiment No. 385 ..... Date .....

Subject ..... Purpose .....

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Data 1	Data2	Data3		Average	Specific	%Specific	%Inhibition
983.4	861.7		296679	923	88	3	97
849.6	823.4			837	2	0	100
975.9	1084.2			1030	195	7	93
1046.6	1018.4			1033	198	7	93
1093.4	1092.4			1093	258	10	90
1161.6	1386.7			1274	439	17	83
2019.2	1991			2005	1170	44	56
2803.4	2994.6			2899	2064	78	22
934.9	989.6		58442	962	127	5	95
975.4	748.3			862	27	1	99
1057.4	1010			1034	199	8	92
1261.5	1040.1			1151	316	12	88
1649.2	1616			1633	798	30	70
2523.9	2586.7			2555	1720	65	35
3257	3123.4			3190	2355	89	11
3856.8	3380.8			3619	2784	106	-6
885.2	802.5		334170	844	9	0	100
1136.5	1138.3			1137	302	11	89
2189.1	2074.5			2132	1297	49	51
3087.3	3050.6			3069	2234	85	15
3532.9	3558.4			3546	2711	103	-3
3764	3539.1			3652	2817	107	-7
3774.1	3618.7			3696	2851	109	-9
3612.3	3697.4			3655	2820	107	-7
2867.9	3213.8		333329	3041	2205	84	16
3777.6	800			2289	1454	55	45
4170.6	1203.1			2687	1852	70	30
3943.3	1546.7			2745	1910	72	28
3740.9	2130.6			2936	2101	80	20
3946.5	2992.3			3469	2634	100	0
3792.8	3364.9			3579	2744	104	-4
3865.1	3664.8			3765	2930	111	-11
3440.6	3190.3		333328	3315	2480	94	-6
3485.2	3792.4			3639	2804	106	-6
3760.8	3731.9			3746	2911	110	-10
3602.8	4130.1			3856	3031	115	-15
4474.9	3668.3			4072	3237	123	-23
3920	3725.3			3823	2989	113	-13
3677.5	3601.8			3640	2805	106	-6
3648.8	3709.3			3679	2844	108	-8
792.9	877.1		58260	835	0	0	100
866	770.3			818	-17	-1	101
998.2	976.9			989	154	6	94
1080.3	1085.7			1083	248	9	91
1099.8	1267.6			1184	349	13	87
1549	1758.8			1654	819	31	69
2612.3	3033.5			2823	1988	75	25
3120.4	3823.6		Control	3472	2637	100	0

Data 1	Data2	Data3
1687.6	1772	
2461.3	2536.1	
3135.9	3279.3	
3478.2	3778	
3542.1	3337	
3536.8	3692.9	
3547.2	3489.4	
3508.5	3706.7	
6302.6	2225.2	
3316.3	3142.6	
3549.3	3500.9	
3626.9	3714	
3552	3873	
3848.8	3985.8	
3610.6	3514.8	
3596.4	3561.1	
1555.4	1466.1	
2316.5	2663.8	
3533.4	3340.9	
3603.7	3471.4	
3694.4	3303.1	
3627.2	3700.2	
3704.3	3673.1	
3710.7	3923.9	
1060.6	1164.6	
1671.4	1626.9	
3200	2702.5	
3148.2	3157.4	
3542.3	3363.7	
3609.6	3645.6	
3676.6	3482.5	
3713.6	3345	
1549.3	1529.5	
2407.1	2157.8	
3066.6	2977.8	
3468.6	3079.8	
3374.2	3251.9	
3470	3006.6	
3578.8	3465.6	
3505.9	3806	
771.8	799.2	
1012	997.2	
968.5	904.7	
1209.9	1085.2	
1270	1371.6	
2044.8	1874.1	
3000	2867.6	
3293.4	3349.6	

	Average	Specific	%Specific	%Inhibition
333592	1730	944	37	63
	2499	1713	68	32
	3208	2422	96	4
	3628	2843	112	-12
	3440	2654	105	-5
	3615	2829	112	-12
	3518	2733	108	-8
	3608	2822	111	-11
333319	4264	3478	137	-37
	3229	2444	96	4
	3525	2740	108	-8
	3670	2885	114	-14
	3719	2927	115	-15
	3917	3132	123	-23
	3563	2777	110	-10
	3579	2793	110	-10
333591	1511	725	29	71
	2490	1705	67	33
	3437	2652	105	-5
	3538	2752	109	-9
	3499	2713	107	-7
	3664	2878	113	-13
	3689	2903	114	-14
	3817	3032	120	-20
333590	1113	327	13	87
	1649	864	34	66
	2951	2166	85	15
	3153	2367	93	7
	3453	2668	105	-5
	3628	2842	112	-12
	3581	2795	110	-10
	3529	2744	108	-8
332556	1539	754	30	70
	2282	1497	59	41
	3022	2237	88	12
	3274	2489	98	2
	3313	2528	100	0
	3238	2453	97	3
	3522	2737	108	-8
	3656	2870	113	-13
58669	786	0	0	100
	1005	219	9	91
	937	151	6	94
	1148	362	14	86
	1321	535	21	79
	1959	1174	46	54
	2934	2148	85	15
Control	3322	2536	100	0

Contd. on page _____ Investigator _____ Date _____

Read and Understood _____ Date _____

Exhibit AQ

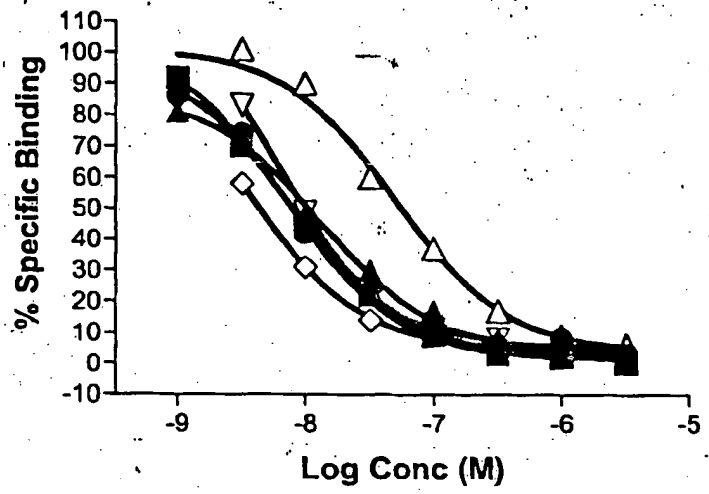
No. 15946- 9

Project No. NPY5 Protocol / Experiment No. 467 Date

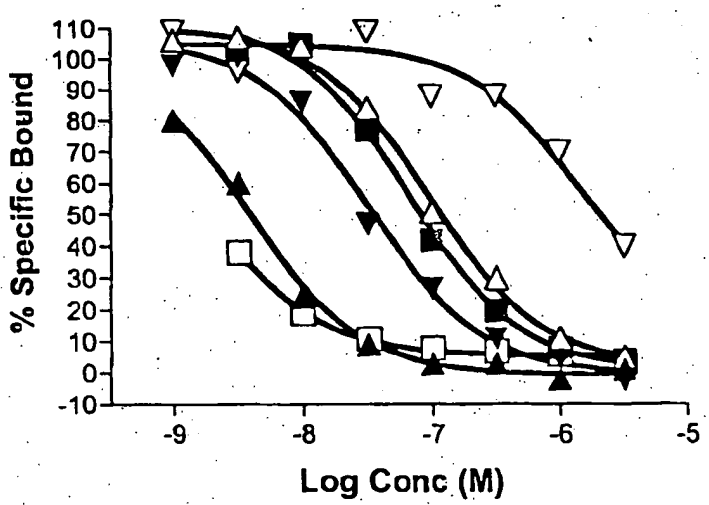
Subject Purpose

Contd. from page

Binding of new compounds to NPY5 receptor



Binding of new compounds to NPY5 receptor



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Read and Understood Date